Notes

Efficient and Solvent-free Preparation of Formate Esters from Alcohols under Microwave Irradiation

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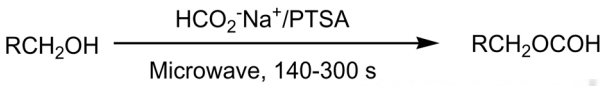
Conversion of alcohols into the corresponding formate esters has been received great attention and numbers of synthetic methods have been developed. For examples, formate esters have been prepared by the reaction of alcohols with formic acid in the presence of a number of reaction promoters such as boron oxide,[1] acetic anhydride,[2] and DCC.[3] Ethyl formate also has been used for the O-formylation of alcohols in the presence of variety catalysts such as $Ce(OTf)_4$,[4] PPh_3/CBr_4,[5] cerium polyoxometalate,[6] and potassium dodecatungstocobaltate trihydrate.[7] In addition, the formylation reaction of alcohols with chloral in the presence of potassium carbonate has been recently reported.[8] However, the majority of the above mentioned methods have one or more drawbacks such as harsh reaction conditions, use of toxic organic solvents, long reaction times, and low yields. Therefore, it is highly desirable to develop new and efficient method avoiding use of toxic reagents and harmful organic solvents for the preparation of formate esters from alcohols.

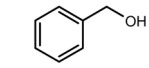
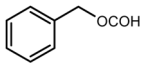
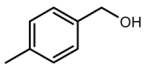
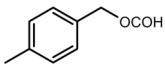
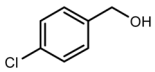
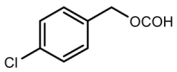
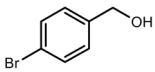
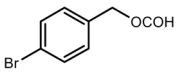
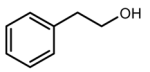
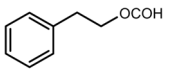
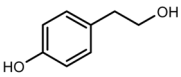
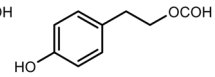
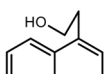
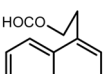
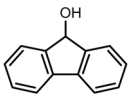
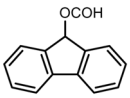
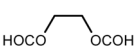
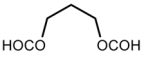
In recent years, there have been considerable interest in the application of microwave irradiation technique to the variety of organic transformations.[9] Microwave-assisted reactions have many advantages such as rapid reaction rates, clean reactions as well as environmentally benign conditions.[10]

Herein, we wish to report the new, facile, and rapid synthesis of the formate esters by the reaction of alcohols with sodium formate and *p*-toluenesulfonic acid monohydrate (PTSA) under microwave irradiation conditions. Treatment of alcohols with 1.5 equivalent of sodium formate and PTSA under microwave irradiation (850 W) for 140-300 sec cleanly afforded the corresponding formate esters in high yields (Scheme 1). All reactions were conducted in a commercial domestic microwave oven (Samsung RE-21C). As shown in the Table 1, both aromatic alcohols and aliphatic alcohols smoothly underwent O-formylation reaction equally well in high yields. Under the present reaction conditions, primary benzylic alcohols with electron-donating or withdrawing groups were readily converted to their corresponding formate esters. It is also important to note that



Scheme 1

Table 1. Formylation of alcohols under microwave irradiation conditions

Entry	Alcohols	Products	Time (sec)	Yield (%)[a]
1			220	85 (**1**)
2			240	81 (**2**)
3			240	83 (**3**)
4			200	84 (**4**)
5			180	81 (**5**)
6			140	86 (**6**)
7			220	84 (**7**)
8			300	78 (**8**)
9	$CH_3(CH_2)_4CH_2OH$	$CH_3(CH_2)_4CH_2OCOH$	160	77 (**9**)
10	$CH_3(CH_2)_7CH_2OH$	$CH_3(CH_2)_7CH_2OCOH$	180	75 (**10**)
11	$CH_3(CH_2)_{10}CH_2OH$	$CH_3(CH_2)_{10}CH_2OCOH$	180	75 (**11**)
12			300	67 (**12**)
13			300	65 (**13**)

[a]Isolated yields

the present protocol is highly selective for the formylation of hydroxyl group of 2-(4-hydroxyphenyl)ethanol without affecting phenolic moiety (entry 6). We have attempted formylation of phenol under present reaction conditions gave only unchanged starting material. Aliphatic diols were also converted successfully into the corresponding formate esters (entries 12-13). When this method was conducted in neat formic acid by replacing of sodium formate/PTSA gave generally complicated product mixture with very low yields of formate esters. Attempted formylation reactions of secondary alcohols such as 1-phenylethanol derivatives were proved to be ineffective under the present conditions to give only complex product mixtures. In consideration of these results, the O-formylation reactions presumably occurred *via* the initial protonation of alcoholic oxygen atom and subsequent S_N2 type displacement reaction with formate nucleophile. When the formylation reactions were conducted in the methylene chloride under reflux for 6 h, the yields were generally 20% lower in average which showed the advantage of the present protocol.

In summary, we have demonstrated that the microwave-assisted reactions of various alcohols with sodium formate and PTSA cleanly and rapidly gave the corresponding formate esters in high yields. We believe this new facile and efficient protocol will serve as a useful alternative to the existing formate ester preparation methods.

Experimental Section

The ^{1}H and ^{13}C spectra were recorded on Varian Gemini 2000 300 MHz NMR spectrometer in $CDCl_3$ with TMS as the internal standard. The IR spectra have been recorded on JASCO FT-IR 5300 FT-IR spectrometer on samples taken as neat or as KBr discs. The mass spectra were recorded on Micromass Autospec spectrometer. All products were characterized by comparison with reported spectral data.[6]

General procedure for the preparation of formate esters: A mixture of an alcohol (1.0 mmol), sodium formate (1.5 mmol), *p*-toluenesulfonic acid monohydrate (1.5 mmol), and dichloromethane (1 mL) was placed in a glass tube. After evaporation of dichloromethane *in vacuo*, the reaction mixture was inserted in an alumina bath inside a domestic microwave oven and irradiated (850 W) 7-15 times for a period of 20 sec with 20 sec intervals. After completion of the reaction, the reaction mixture was extracted with dichloromethane (2 × 25 mL), washed with water, and dried over $MgSO_4$. After evaporation of solvent, the product was purified by column chromatography on silica gel (Merck 100-200 mesh, ethyl acetate-hexane, 1:3) to give the corresponding formate ester.

Benzyl formate (1). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.40 (m, 5H), 5.22 (s, 2H); ^{13}C NMR ($CDCl_3$) 70.6, 127.1, 127.7, 129.0, 141.2, 160.7; FT-IR (neat) 3030, 2930, 1725, 1452, 1171 cm^{-1}; Ms m/z (%) 136 (M^+, 50), 91 (100), 77 (50).

4-Methylbenzyl formate (2). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.17 (m, 4H), 5.17 (s, 2H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$) 24.3, 70.6, 127.0, 129.2, 137.3, 138.2, 160.7; FT-IR (neat) 3030, 2927, 1727, 1455, 1174 cm^{-1}; Ms m/z (%) 150 (M^+, 85), 105 (100), 77 (75).

4-Chlorobenzyl formate (3). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.33 (m, 4H), 5.16 (s, 2H); ^{13}C NMR ($CDCl_3$) 70.6, 128.5, 129.0, 133.2, 139.3, 160.7; FT-IR (neat) 3030, 2926, 1728, 1453, 1172 cm^{-1}; Ms m/z (%) 170 (M^+, 70), 141 (15), 125 (100), 77 (80).

4-Bromobenzyl formate (4). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.16 (m, 4H), 5.07 (s, 2H); ^{13}C NMR ($CDCl_3$) 70.6, 122.0, 129.3, 131.8, 140.2, 160.7; FT-IR (neat) 3030, 2927, 1726, 1454, 1172 cm^{-1}; Ms m/z (%) 213 (M^+, 46), 169 (60), 107(58), 89 (100), 77(45).

Phenethyl formate (5). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.21 (m, 5H), 4.38 (t, 2H), 2.97 (t, 2H); ^{13}C NMR ($CDCl_3$) 34.6, 63.9, 126.4, 128.2, 128.6, 138.1, 160.6; FT-IR (neat) 3030, 2936, 1724, 1498, 1455, 1170 cm^{-1}; Ms m/z (%) 150 (M^+, 26), 104 (100), 91(50), 77(8).

2-(4-Hydroxyphenyl)ethyl formate (6). Colorless crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.08 (d, 2H), 6.78 (d, 2H), 5.55 (s, 1H), 4.34 (t, 2H), 2.90 (t, 2H); ^{13}C NMR ($CDCl_3$) 33.9, 64.9, 115.4, 129.0, 129.9, 154.5, 161.6; FT-IR (KBr) 3403, 1717, 1614, 1516, 1220, 1172 cm^{-1}; Ms m/z (%) 166 (M^+, 10), 120 (100), 107 (60), 77 (20).

2-(1-Naphthyl)ethyl formate (7). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.74 (m, 3H), 7.34 (m, 4H), 4.49 (t, 2H), 3.43 (t, 2H); ^{13}C NMR ($CDCl_3$) 31.6, 63.5, 123.0, 125.1, 125.4, 125.9, 126.7, 127.3, 128.5, 131.6, 132.9, 133.5, 160.6; FT-IR (neat) 3047, 2951, 1717, 1597, 1510, 1464, 1397, 1171 cm^{-1}; Ms m/z (%) 200 (M^+, 18), 154 (100), 141 (83).

9-Fluorenyl formate (8). Colorless crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.67 (d, 2H), 7.55 (d, 2H), 7.42 (t, 2H), 7.30 (t, 2H), 6.89 (s, 1H); ^{13}C NMR ($CDCl_3$) 74.5, 119.9, 125.7, 127.7, 129.5, 140.9, 141.2, 161.4; FT-IR (KBr) 3005, 2926, 1715, 1453, 1310, 1155, 926, 757, 735 cm^{-1}; Ms m/z (%) 210 (M^+, 64), 182 (45), 181 (58), 165 (100).

***n*-Hexyl formate (9).** Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 1H), 4.13 (t, 2H), 1.63 (m, 2H), 1.29 (m, 6H), 0.86 (t, 3H); ^{13}C NMR ($CDCl_3$) 14.1, 22.7, 25.5, 28.6, 31.5, 67.4, 160.7; FT-IR (neat) 2926, 2855, 1731, 1466, 1376, 1175 cm^{-1}; Ms m/z (%) 84 (36), 69 (58), 56 (100).

***n*-Nonyl formate (10).** Colouless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 4.16 (t, 2H), 1.66 (m, 2H), 1.28 (m, 12H), 0.88 (t, 3H); ^{13}C NMR ($CDCl_3$) 13.9, 22.5, 25.7, 28.4, 29.1, 29.4, 31.7, 63.9, 161.0; FT-IR (neat) 2926, 2856, 1731, 1467, 1378, 1170 cm^{-1}; Ms m/z (%) 126 (20), 98 (41, 70 (76), 56 (100).

***n*-Dodecyl formate (11).** Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 4.16 (t, 2H), 1.66 (m, 2H), 1.28 (m, 18H), 0.88 (t, 3H); ^{13}C NMR ($CDCl_3$) 13.9, 22.6, 25.7, 28.4, 29.1, 29.2, 29.5, 31.8, 63.8, 160.9; FT-IR (neat) 2925, 2854, 1731, 1467, 1377, 1179 cm^{-1}; Ms m/z (%) 168 (40), 140 (56), 111(60), 83 (96), 55(100).

Ethylene glycol diformate (12). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 2H), 4.36 (s, 4H); ^{13}C NMR ($CDCl_3$) 65.4, 160.7; FT-IR (neat) 2926, 1735, 1465,

1176 cm^{-1}; Ms m/z (%) 72 (15), 60 (100).

Propane-1,3-diyl diformate (13). Colorless liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 2H), 4.26 (t, 4H), 2.05 (m, 2H); ^{13}C NMR ($CDCl_3$) 27.0, 63.6, 160.7; FT-IR (neat) 2927, 1736, 1465, 1176 cm^{-1}; Ms m/z (%) 86 (10), 74 (15), 57 (100).

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